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CASE REPORT | LIVER

Multiple Myeloma Presenting as Acute Liver Failure

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ABSTRACT

Liver failure is rarely caused by multiple myeloma (MM). We present an unusual case of MM initially presenting as acute liver injury. A 79-year-old man with new-onset fatigue, decreased appetite, and no history of liver disease was found to have evidence of hepatic decompensation. Liver biopsy demonstrated diffuse plasma cell infiltration, and MM was confirmed with bone marrow biopsy. Chemotherapy was initiated, but the patient decompensated and died due to respiratory failure. MM should be considered on the differential for acute decompensated liver disease. Hepatic involvement of MM at presentation is a poor prognostic indicator, and prompt initiation of treatment can be life-saving.

INTRODUCTION

Liver failure caused by multiple myeloma (MM) is uncommon. Any clinical involvement of the liver at the time of initial diagnosis of MM is also rare. Hepatic involvement, if present, is normally discovered later during the course of disease.[1] The majority of cases reporting liver failure in MM are secondary to amyloid deposition as opposed to plasma cell infiltration.[2-4] Genetic characteristics of MM that indicate aggressive disease and poor prognosis are more often present in disease that affects the gastrointestinal (GI) tract.[1]

CASE REPORT

A robust 79-year-old Iranian man with hypertension, diabetes mellitus type 2, and a history of nephrolithiasis presented to his primary care physician with increasing fatigue, decreased appetite, and early satiety worsening over 1 month. He had no previous history of liver disease and denied alcohol use, travel outside of the United States, and risk factors for viral hepatitis. Daily medications included metformin, metoprolol, and amlodipine. Laboratory tests revealed an elevated serum creatinine (2.6 mg/dL), and the patient was advised to present to the emergency department for evaluation and treatment of acute kidney injury. On presentation, further testing showed total bilirubin 3.1 mg/dL, direct bilirubin 2.7 mg/dL, alanine aminotransferase 68 U/L, aspartate aminotransferase 116 U/L, alkaline phosphatase 218 U/L, and a platelet count of 54,000/μL. Abdominal imaging with ultrasound and computed tomography (CT) revealed a coarse liver echotexture with patent vasculature and splenomegaly. No biliary duct dilatation was noted.

A work-up for presumed cirrhosis was initiated. Tests for hepatitis A, B, and C, Epstein-Barr virus, and cytomegalovirus were negative, as were autoantibodies. Acetaminophen blood level was undetectable, and alpha-1 antitrypsin was normal. Amlodipine was considered a potential culprit medication; however, when this was discontinued, hepatic function continued to worsen. A diagnosis of decompensated non-alcoholic steatohepatitis was suspected.

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Figure 1. T2-weighted magnetic resonance cholangiopancreatography showing splenomegaly with no evidence of cirrhosis and no biliary system abnormalities.

Bilirubin continued to rise acutely during hospitalization, with total bilirubin measuring 10.6 g/dL (direct 8.0 g/dL) on hospital day 8. Magnetic resonance imaging and T2-weighted magnetic resonance cholangiopancreatography revealed splenomegaly with no evidence of cirrhosis or biliary abnormality (Figure 1). Atypical cells were discovered on peripheral blood smear; metamyelocytes, atypical lymphocytes, and dysmorphic red blood cells suggested an infiltrative disease as the cause of liver injury. Liver biopsy revealed extensive involvement of plasma cell neoplasm and surrounding liver parenchyma with minimal steatosis and no evidence of fibrosis (Figure 2).

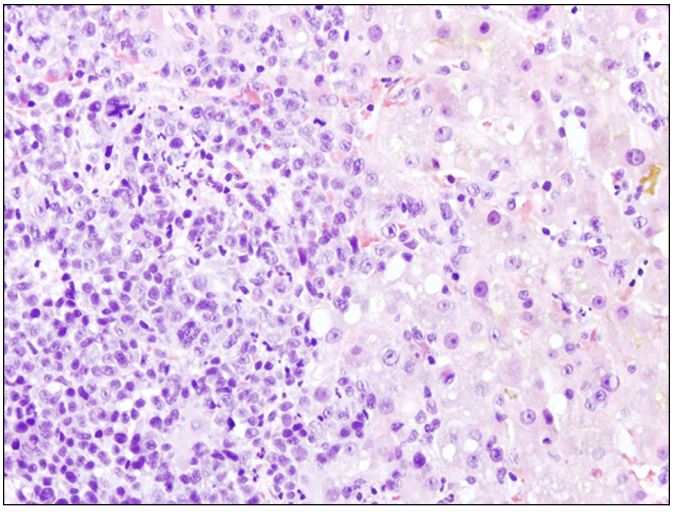

Figure 2. Liver parenchyma showing extensive neoplastic plasma cell infiltration and cholestasis (hematoxylin and eosin stain, 400x).

Figure 3. Positron emission tomography-computed tomography scan demonstrating a heterogenous fluorodeoxyglucose (FDG)-avid liver, an intensely FDG-avid spleen, and no lymph node involvement. Bone marrow of the axial and proximal appendicular skeleton is diffusely involved.

Subsequent bone marrow biopsy confirmed the diagnosis of MM with 90% kappa-restricted plasma cells. Cytogenetics showed a complex karyotype. Positron emission tomography (PET)-CT imaging demonstrated heterogenous fluorodeoxyglucose (FDG)-avid liver, intensely FDG-avid spleen, and no lymph node involvement. Bone marrow of the axial and proximal appendicular skeleton was diffusely involved, indicating stage III plasmablastic disease (Figure 3). Serum studies showed free kappa light chains.

Chemotherapy was initiated on hospital day 18, but options were limited due to elevated total bilirubin 30.6 mg/dL (direct 22.7 mg/dL) at this time. A modified protocol was built; dexamethasone, dose-reduced bortezomib, and melphalan were administered. Lenalidomide was contraindicated with this level of bilirubin.

Despite initiation of chemotherapy, the patient continued to decompensate. He developed ascites, anasarca, and encephalopathy with asterixis. On hospital day 24, platelet

Table 1. Previously reported cases of multiple myeloma leading to acute liver failure

	Age	Sex	Ethnicity	Initial Presentation/Type of Liver Involvement	Intervention	Outcome of Liver Function
Rahhal et al.[5]	49	M	African American	Acute renal failure with normal liver function Developed liver failure after 1 month of treatment Liver biopsy: plasma cells, kappa expressing	Thalidomide and dexamethasone: no response Switched to bortezomib	Liver failure 3 months after diagnosis Survival time: 4 months
Barth et al.[6]	88	F	German	Painless jaundice and elevated transaminases Liver biopsy showed plasma cells, lambda expressing	Prednisolone	Rapid improvement
Yağcí et al.[7]	69	M	Turkish	Back pain and lytic bone lesions Developed liver failure after 2 weeks of treatment Autopsy: plasma cell infiltration, kappa expressing	Vincristine, doxorubicin and dexamethasone	Liver failure 7 months after diagnosis Survival time: 7.5 months

transfusion was done for thrombocytopenia and preparation for therapeutic paracentesis. Shortly thereafter, pulmonary edema and acute respiratory failure developed and was refractory to diuretics and oxygen therapy. The patient declined intubation and died due to respiratory failure.

DISCUSSION

The prevalence of MM leading to evidence of liver dysfunction is 0.4%, with only 3 case reports of MM leading to acute liver failure (Table 1).[1,5-7] In up to 40% of cases of MM, there is some degree of plasma cell infiltration of the liver; however, this is usually clinically silent and discovered on autopsy or incidentally on imaging.[1,8] It is rare to have evidence of hepatic involvement on initial presentation. Talamo et al. reported only 11 out of 2,584 patients with tissue-documented hepatic involvement of MM; only 1 patient developed liver failure, 2 had elevated bilirubin (the highest being 8 mg/dL), and the remainder were asymptomatic.[1] Our patient had a bilirubin of 3.1 mg/dL on admission and peaked at 40 mg/dL within 2 weeks.

Mechanisms of liver failure secondary to MM include direct invasion of plasma cells, plasmacytoma, light chain deposition, or amyloid deposition (the latter being the most prevalent).[1,2,9] MM involving the liver more commonly occurs as an infiltrative disease, which is not radiologically detectable. Nodular involvement is less common and is suggestive of plasmacytomas.[3] Complex karyotype, specifically monosomy 13, is the strongest indicator of poor prognosis in MM. Monosomy 13 is more prevalent when MM invades the GI tract, therefore associating GI system involvement with a poor prognosis.[1]

In cases of MM presenting with liver injury, it is suspected that the survival rate is much lower, due to major limitations in safely administering chemotherapy in patients with liver dysfunction. Importantly, hepatotoxicity and liver failure are potential consequences of chemotherapy for MM, even in patients whose liver function is normal upon diagnosis. Common therapeutic options for newly diagnosed MM include combinations of proteasome inhibitors bortezomib and carfilzomib, thalidomide and its analog lenalidomide, cyclophosphamide, dexamethasone, and less commonly the anthracycline doxorubicin. Several of these agents are contraindicated or require dose adjustment for hepatic impairment.[10]

Upon retrospective review of our case, there were no clear indicators that MM should have been suspected. Although the patient had evidence of acute renal failure, his calcium level was normal and there was no protein gap or evidence of pathological bone disease. In this case, worsening cholestasis rapidly progressing to overt liver failure without an obvious explanation was the only indicator of MM. This phenomenon has been reported only 3 times in the literature.[5-7]

It is evident that MM clinically affecting the liver carries a very poor prognosis. It is important to suspect infiltrative liver diseases, including MM, as a cause of liver damage early in the course of disease. Many chemotherapy agents used to treat MM involve metabolism through the liver. Therefore, prompt initiation of treatment is essential to improve survival.

DISCLOSURES

Author contributions: S. Cull and D. Westrich wrote the manuscript. R. Bhatia edited the manuscript. J. Lai assessed the pathology. AS Befeler reviewed and supervised the manuscript. S. Cull is the article guarantor.

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Numerous unsuccessful attempts were made to contact the deceased patient's family for informed consent. All identifying information has been removed to protect patient privacy.

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